

#4

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PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant: Weigel et al) Atty Dkt No: 5820.603
Serial No: 09/842,930)
Filed: April 25, 2001)
For: IDENTIFICATION AND USES)
OF A HYALURONAN)
RECEPTOR FOR)
ENDOCYTOSIS)

Box Missing Parts
Commissioner for Patents
Washington, D.C. 20231

PRELIMINARY AMENDMENT

Applicant herein seeks to amend the above referenced application as shown below, prior to the first examination and action of the United States Patent and Trademark Office, in response to the Notice to File Missing Parts of Nonprovisional Application mailed June 25, 2001.

In the Drawings:

Please accept the formal Drawings filed herewith.

In the Specification:

Please amend Tables III-V of the Specification (located on pages 94-96 of the Specification) as submitted on the following pages in clean, replacement form. Also, following the Remarks section are redline, marked-up versions of such tables illustrating the amendments made thereto.

Table III

Oligonucleotide Primers Used for RT-PCR Analysis and DNA Sequencing

| Primer | SEQ ID NO: | Sequence | Position | PCR Product (bp) | Peptide Sequences confirmed |
|--------|------------|---------------------------|-----------|------------------|-----------------------------|
| BAB1F | 5 | TCAATATAATCTGGCGAATGCAAT | 3-26 | | |
| HSP2R | 7 | AGTTCCGAATGGGCGAGGTCAGCTC | 397-420 | 418 | 3 |
| BAB3F | 26 | ATGAGGAAGCTCGGGTTAAAG | 1452-1472 | | |
| BAB4R | 29 | GATGTAGCCATTGTTTGTGTCGCAA | 1769-1792 | 341 | 2 |
| HSP2F | 33 | GAGCTGACCTGCCCATTCGGAAC | 397-420 | | |
| HSP3R | 35 | CTTTAACCCGAGCTTCCTCAT | 1452-1472 | 1076 | 4 |
| BAB6F | 30 | AGACGCCAAATGTGTGACCTCCA | 3078-3101 | | |
| BAB7R | 31 | GAATAGGCCAGCACTTCCGTCAGG | 3510-3533 | 456 | 2 |
| BAB1F | 5 | TCAATATAATCTGGCGAATGCAAT | 3-26 | | |
| BAB10R | 32 | GGTGAGGCAGTTGGCGCTGGTATG | 851-874 | 872 | 3 |
| HSP2F | 33 | GAGCTGACCTGCCCATTCGGAAC | 397-420 | | |
| BAB10R | 32 | GGTGAGGCAGTTGGCGCTGGTATG | 851-874 | 478 | 3 |
| BAB10F | 34 | CATACCAGCGCCAACTGCCTCACC | 851-874 | | |
| HSP3R | 35 | CTTTAACCCGAGCTTCCTCAT | 1452-1472 | 622 | 3 |
| BAB9F | 36 | CAAGTACGGCATCCACTGTGACCA | 697-720 | | |
| HSP3R | 35 | CTTTAACCCGAGCTTCCTCAT | 1452-1472 | 776 | 3 |

Other Primers used for RT-PCR and sequencing.

| Name | SEQ ID NO: | Sequence | Position |
|------|------------|--------------------------|-----------|
| 5F | 37 | GGCTACTTCGGGCGAGACTGTCAG | 2386-2409 |
| 5R | 38 | CTGACAGTCTCGCCCGAAGTAGCC | 2386-2409 |
| 8F | 39 | TTGTACTCTTCAGCTGGCACC | 4406-4426 |
| 8R | 6 | GGTGCCAGCTGAAGAGTACAA | 4406-4426 |

Table IV

Summary of Amino Acid Sequences Derived From Peptides of the
Purified Human 190 kDa HARE Protein

The human HARE proteins were immuno-affinity-purified from human spleen, subjected to SDS-PAGE and the 190 kDa protein band was excised and analyzed for internal peptide sequence following trypsin digestion. The amino acid sequences of these ten tryptic peptides were highly homologous or identical to the sequences of the rat 175 kDa HARE, reported herein above, and seven of these (not in bold face) were identical to regions within a human hypothetical protein of unknown expression and unknown function under GenBank accession number BAB15793. HARE peptides in boldface were not in the ORF for BAB15793.

| Peptide Designation | Amino Acid Sequences | Start-End Residue | SEQ ID NO: |
|-------------------------------|-------------------------|-------------------|------------|
| PR 1822 | XSKPK | 758-761 | 40 |
| PR 1823 | LTFDK | 1054-1058 | 41 |
| PR 1825-1 st | GSYQELPK | 440-448 | 42 |
| PR 1825-2 nd | GTLFVPQNSGLGE | 1198-1210 | 43 |
| PR 1826 | DLVGPGPFTVFAPLSAAFDEEAR | 466-488 | 44 |
| PR 1869-1st | ELTSPFGTK | 133-141 | 45 |
| PR 1869-2 nd | MPQVLR | 498-503 | 46 |
| PR 1870 | SPLGQYK | 1047-1053 | 47 |
| PR 1871-1st | VLEIQK | 107-112 | 48 |
| PR 1872 | VIHGLGK | 100-106 | 49 |

Table V

**Molecular Mass Mapping of Peptides Derived From the
Human 190 kDa HARE Protein**

THE MOLECULAR MASSES OF SEVEN PEPTIDES DERIVED FROM TRYPTIC DIGESTION OF THE PURIFIED HUMAN 190 kDa HARE PROTEIN WERE DETERMINED BY MALDI-TOF MASS SPECTROMETRY AT THE LOUISIANA STATE UNIVERSITY PROTEIN CHEMISTRY FACILITY CORRESPONDED WITH PERFECT IDENTITY TO DEDUCED SEQUENCES WITHIN A PREDICTED HUMAN PROTEIN OF UNKNOWN FUNCTION (ACCESSION NUMBER BAB15793). THE MONOISOTOPIC PEPTIDE MASSES WERE SEARCHED AGAINST ENTRIES IN THE DATABASE, USING PEPTIDSEARCH SOFTWARE FROM THE EMBL PROTEIN AND PEPTIDE GROUP. IDENTICAL MASSES ARE ASSIGNED IN THIS SEARCH IF THE DIFFERENCE BETWEEN THE OBSERVED AND PREDICTED (CALCULATED) MASSES FOR A PEPTIDE IS < 0.2 Da. THE CORRESPONDING STARTING AND ENDING RESIDUES FOR EACH PEPTIDE WITHIN THE DEDUCED PROTEIN SEQUENCE IS SHOWN. THE N-TERMINAL R OR K RESIDUES IN PARENTHESES INDICATE THE DEDUCED RESIDUE IN THE PROTEIN AND CONFIRM THAT TRYPSIN DIGESTION OCCURRED ON THE C-TERMINAL SIDE OF THOSE AMINO ACIDS AS EXPECTED.

| Measured Mass (Da) | Calculated Mass (Da) | Mass Difference (Da) | Start-End Residues | Sequence in Deduced Human | SEQ ID NO: |
|--------------------|----------------------|----------------------|--------------------|---------------------------|------------|
| 599.273 | 599.294 | -0.021 | 796-800 | (K)GYFGR | 50 |
| 671.384 | 671.399 | -0.015 | 656-660 | (K)FHVIR | 51 |
| 792.621 | 792.426 | 0.195 | 1047-1053 | (R)SPLGQYK | 52 |
| 1034.621 | 1034.552 | 0.068 | 440-448 | (R)GSIYQELPK | 53 |
| 1061.781 | 1061.584 | 0.196 | 677-686 | (K)TLQGSELSVK | 54 |
| 1624.051 | 1623.886 | 0.165 | 1047-1060 | (R)SPLGQYKLTFDKAR | 55 |
| 1092.771 | 1092.588 | 0.183 | 495-503 | (K)YGLMPQVLR | 56 |

In the Sequence Listing:

Please delete the Sequence Listing submitted on pages 139-207 of the Specification and substitute therefore the substitute Sequence Listing filed herewith under 37 CFR 1.825. The Sequence Listing filed with the application on April 25, 2001 did not contain a SEQ ID NO:37, and therefore the substitute Sequence Listing submitted herewith has been renumbered so that SEQ ID NOs:38-57 are now SEQ ID NOs:37-56. The Specification has been amended herein above to also reflect such renumbering of the SEQ ID NOs. In addition, the substitute Sequence Listing has been reformatted to fully comply with 37 CFR 1.821-1.823. The substitute Sequence Listing contains no new matter.

Also submitted herewith is a substitute copy of the Computer Readable Form of the substitute Sequence Listing under 37 CFR 1.825 which fully complies with the requirements of 37 CFR 1.821-1.824. The Computer Readable Form contains all previously submitted data with the above requested amendments incorporated therein. The copy of the Sequence Listing in Computer Readable Form is the same as the substitute copy of the Sequence Listing filed herewith.

REMARKS

This is meant to be a complete response to the Notice to File Missing Parts of NonProvisional Application mailed June 25, 2001. In the Notice to File Missing Parts, it was noted that the oath or declaration was missing. In addition, the application was considered informal since it does not comply with the regulations, and the required items identified below were required to be timely submitted to avoid abandonment:

- (1) substitute drawings in compliance with 37 CFR 1.84 because the drawing sheets did not have the appropriate margins;
- (2) a statement that the content of the sequence listing information recorded in computer readable form is identical to the written sequence listing and, where applicable, includes no new matter;
- (3) a substitute computer readable form (CRF) copy of the Sequence Listing, as the content of the computer readable form does not comply with the requirements of 37 CFR 1.822 and/or 1.823, and a statement that the content of the sequence listing information recorded in computer readable form is identical to the written sequence listing and, where applicable, includes no new matter.

In response to the Notice to File Missing Parts, submitted herewith are a properly signed oath/declaration in compliance with 37 CFR 1.63 and formal Drawings having the appropriate margins.

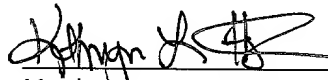
Also in response to the Notice to File Missing Parts, the Sequence Listing submitted on Pages 139-207 of the Specification and in Computer Readable Form, was reviewed. In addition to the fact that such copies of the Sequence Listing did not comply with the requirements of 37 CFR 1.822 and/or 1.823, as noted in the Notice to File Missing Parts, it was noted that no SEQ ID NO:37 appeared in the Sequence Listing or the disclosure contained in the Specification. Therefore, a substitute written copy of the Sequence Listing is submitted herewith in compliance with 37 CFR 1.825. Such substitute Sequence Listing has been amended to fully comply with 37 CFR 1.822 and 1.823, and SEQ ID NOs:38-57 have been renumbered as SEQ ID NOs:37-56. The substitute written copy of the Sequence Listing contains no new matter. In addition, a substitute copy of the Computer Readable Form of the Sequence Listing is submitted herewith which includes all previously submitted data and has been amended to fully comply with 37 CFR 1.822 and 1.823, and SEQ ID NOs:38-57 have been renumbered as SEQ ID NOs:37-56. The substitute copy of the Sequence Listing in computer readable form is identical to the substitute copy of the Sequence Listing in written form submitted herewith.

In addition, the Specification has been amended herein to renumber SEQ ID NOs:38-57 as SEQ ID NOs:37-56, for the reasons explained herein above in regards to the Sequence Listing. No substantive changes have been made in the application and such amendments do not introduce any new matter. Applicant respectfully requests that such amendments be entered into the

record.

Should the Examiner have any questions or comments concerning the before-mentioned amendments to the application or any other matter, Applicant's agent will welcome the opportunity to discuss same with the Examiner.

Respectfully submitted,



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Oklahoma City, Oklahoma 73114
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Agent for Applicant

MARKED-UP VERSION OF THE PARAGRAPHS OF THE SPECIFICATION
SHOWING THE CHANGES MADE THERETO

Table III

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| Primer | SEQ ID NO: | Sequence | Position | PCR Product (bp) | Peptide Sequences confirmed |
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| Name | SEQ ID NO: | Sequence | Position |
|------|----------------|--------------------------|-----------|
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| 5R | [39] <u>38</u> | CTGACAGTCTCGCCCGAAGTAGCC | 2386-2409 |
| 8F | [40] <u>39</u> | TTGTACTCTTCAGCTGGCACC | 4406-4426 |
| 8R | 6 | GGTGCCAGCTGAAGAGTACAA | 4406-4426 |

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| PR 1826 | DLVGPGPFTVFAPLSAAFDEEAR | 466-488 | [45] <u>44</u> |
| PR 1869-1st | ELTSPFGTK | 133-141 | [46] <u>45</u> |
| PR 1869-2 nd | MPQVLR | 498-503 | [47] <u>46</u> |
| PR 1870 | SPLGQYK | 1047-1053 | [48] <u>47</u> |
| PR 1871-1st | VLEIQK | 107-112 | [49] <u>48</u> |
| PR 1872 | VIHGLGK | 100-106 | [50] <u>49</u> |

Table V

**Molecular Mass Mapping of Peptides Derived From the
Human 190 kDa HARE Protein**

The molecular masses of seven peptides derived from tryptic digestion of the purified human 190 kDa HARE protein were determined by MALDI-TOF mass spectrometry at the Louisiana State University Protein Chemistry Facility corresponded with perfect identity to deduced sequences within a predicted human protein of unknown function (accession number BAB15793). The monoisotopic peptide masses were searched against entries in the database, using PeptideSearch software from the EMBL Protein and Peptide Group. Identical masses are assigned in this search if the difference between the observed and predicted (calculated) masses for a peptide is < 0.2 Da. The corresponding starting and ending residues for each peptide within the deduced protein sequence is shown. The N-terminal R or K residues in parentheses indicate the deduced residue in the protein and confirm that trypsin digestion occurred on the C-terminal side of those amino acids as expected.

| Measured Mass (Da) | Calculated Mass (Da) | Mass Difference (Da) | Start-End Residues | Sequence in Deduced Human | SEQ ID NO: |
|--------------------|----------------------|----------------------|--------------------|---------------------------|----------------|
| 599.273 | 599.294 | -0.021 | 796-800 | (K)GYFGR | [51] <u>50</u> |
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